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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/454,223	12/09/99	KURNBLUTH R	[illegible]

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EXAMINER	
SEHARASEYON, J	

ART UNIT	PAPER NUMBER
1647	10

DATE MAILED: 08/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILED W/P

Office Action Summary	Application No. 09/454,223	Applicant(s) KORNBLUTH, RICHARD S.	
	Examiner Jegatheesan Seharaseyon	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 9-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This office action is in response to the election filed on 6/15/01 (Paper No: 8) and amendment filed on 7/5/01 (Paper No: 9.). Applicant's election of claims 7 and 8 with traverse (for Groups I and II) is acknowledged. Also acknowledged is the election of human CD40L-SPD (SEQ ID NO: 2) as the species prototype. The traversal is on the ground(s) that only living cells can produce a protein this complex requiring a nucleotide template to synthesize the protein. Thus, the applicant claims that the protein cannot be synthesized by chemical means. Even if this argument was valid, the searches for the two groups will be non-coextensive. In addition, searching for more than one SEQ ID NO. per application would be a burden on the office. Thus, the restriction requirement is deemed proper and is therefore made **FINAL**. Currently, claims 7 and 8 are under consideration. Claims 1-6 and 9-15 are withdrawn from further consideration pursuant to 37 CFR1.142(b) as being drawn to nonelected invention, there being no allowable generic or linking claim.

Drawings

2. The drawing(s) filed on 12/9/99 has been objected to by the draftsperson (see PTO 948). Appropriate correction is required.

Specification

3. The disclosure is objected to because of the following informalities:

3a. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3b. Applicants have cited several references. However, most of the citations are incomplete. For example, in page: 28 line 10, page: 31 lines 22 and 23.

3c. It is unclear what dilutions are used in page: 21 line 20.

3d. It is also unclear what the specification is referring to in page: 3 lines 14 and 24, page: 25 line 9, page: 27 line 19 and page: 31 line 24 by the various symbols used.

3e. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page: 35). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

3f. The table on page 16 lacks a table number.

3g. On page 39, line 3 the word "functional" is misspelled as "funtional".

Appropriate correction is required.

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). See pages 21(lines1-10), 22 (lines 19 and 23) and 23 (lines 10-14 and 25). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) under 35 U.S.C. §§ 131 and 132. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claims 7 and 8 are rejected as vague and indefinite for reciting the terms TNFSF-SPD, LTA, TNFF, LTB and TNFSF4 to TNFSF18, because the full meaning of an acronym should be spelled out at its first use in the claims.

5b. Claim 7 is rejected as being vague and indefinite in the recitation of the term " TNFSF moiety". It is unclear what TNFSF moieties are encompassed in the instant claim. Therefore, the metes and bounds of the claim are unclear. Claim 8 is rejected insofar as it depends on rejected claim 7.

5c. Claim 7 recites the limitation "said ligand strand" in line 19. There is insufficient antecedent basis for this limitation in the claim. Claim 8 is rejected insofar as it depends on rejected claim 7.

5d. Claim 7 recites the limitation "said conjoined collectin strands" in line 21. There is insufficient antecedent basis for this limitation in the claim. Claim 8 is rejected insofar as it depends on rejected claim 7.

5e. Claim 7 is rejected as being vague and indefinite in the recitation of the term " carbohydrate recognition domains (CRD)". It is unclear what sequences are encompassed in the carbohydrate recognition domains. Therefore, the metes and

bounds of the claim are unclear. Claim 8 is rejected insofar as it depends on rejected claim 7.

5f. Claim 7 is rejected as being indefinite because the claim recites "first trimer conjoined to a second polypeptide". It is unclear if this phrase is directed to encompass different polypeptide in the second position. Therefore, the metes and bounds of the claim are unclear. Claim 8 is rejected insofar as it depends on rejected claim 7. This rejection maybe overcome by changing "a" to "the" in line 18 (page 38)..

5g. Claim 8 is rejected as being vague and indefinite in the recitation of the term "functional equivalents". It is unclear what "functional equivalents" are encompassed in the instant claim. Therefore, the metes and bounds of the claim are unclear.

5h. Claims 8 is rejected as being vague and indefinite because of the recitation of the phrase "modification thereof". This language is vague and indefinite since it encompasses potentially any modification to any TNFSF molecule. Therefore, the metes and bounds of the claim are unclear.

Claim Rejections - 35 USC § 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6a. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses the human and murine CD40L, T147N modification of CD40L and RANKL/TRANCE polypeptides (page: 21, line 18 to page: 24, line 2). This meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose polypeptide sequences of the other TNFSF proteins or their functional equivalents and modification thereof. The claims as written, however, encompass polypeptide sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 7 and 8. The specification does not provide written to support the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of the polypeptides CD40L, T147N modification of CD40L and RANKL/TRANCE, the skilled artisan cannot envision all the detailed chemical structure of the claimed polypeptides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the polypeptides CD40L, T147N modification of CD40L and RANKL/TRANCE, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various polypeptide sequences set forth in claims 7 and 8.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

6b. Claims 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for CD40L-SPD, T146N-CD40L-SPD and RANKL/TRANCE-SPD fusion protein does not reasonably provide enablement for other fusion polypeptides consisting of TNFSF functional equivalents, and modifications thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is

sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims read on all TNFSF–SPD functional equivalents and modifications. However, other than CD40L-SPD, T147N-CD40L-SPD and RANKL/TRANCE -SPD fusion polypeptide, the specification as filed fails to disclose any other fusion polypeptide.

Despite knowledge in the art for producing functional equivalents and modifications the specification fails to provide any guidance regarding the generation of the fusion proteins and yet retain the function. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. Therefore, predicting which TNFSF–SPD functional equivalents and modifications containing fusion polypeptides would retain the functions of the protein is well outside the realm of routine experimentation. Thus, undue amount of experimentation would be required to generate changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicants have not taught how one of skill in the art would use the full scope of fusion proteins encompassed by the invention of claims 7 and 8. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences. Given the breadth of claims 7 and 8 in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

7. No claims are allowable but they are apparently free of prior art.

8. The following art are considered closest prior art to applicant's disclosure and raises no issues of patentability under 35 USC 102 or 103 (a) :

Kornbluth et al. Proc. Natl. Acad. Sci., USA 95:5205-5210, 1998.

Hoppe et al. U.S. Patent No: 6,190,886.

McDyer et al. J. Imm. 162: 3711-3717, 1999.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS
August 13, 2001

Gary L. Kunz
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